THE EFFECTS OF DORIDEN ON CONCENTRATIVE ATTENTION SPAN AND PROBLEM SOLVING ABILITY IN MICE

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THE EFFECTS OF DORIDEN ON CONCENTRATIVE ATTENTION SPAN AND PROBLEM SOLVING ABILITY IN MICE

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To overcome resistance and enable the patient to free-associate is one of the outstanding problems of psychotherapy. The therapist seeks information that may have been repressed to avoid anxiety. It is therefore reasonable that a decrease of anxiety would lead to a decreased need for repression. Sedatives and hypnotic drugs are used extensively to assist the patient to overcome his resistance and inability to communicate significant material in the therapeutic situation. The most serious objections to their continued use, particularly in psychoneurotic individuals for whom they are frequently prescribed, are the development of a dependence and possible addiction and habituation. Dependence and habituation on these drugs can be prevented when appropriate precautionary measures are taken by the therapist. Other possible objections could be the unknown effects of these drugs on other processes such as nervous system function and fetal development. Because of these serious objections the promiscuous use of sedatives is to be avoided, particularly, until more is known of their effects.

The sedatives and hypnotics are used in the treatment of simple insomnia, neurasthenia, hysteria, hyperthyroidism, chorea, mental disturbances, and similar conditions where
prompt suppression of excitement and nervousness is desirable. Because of the weak analgesic action of hypnotic and sedative drugs, however, they are of little value in the presence of pain. The sedatives and hypnotics are less potent than the barbituric acid derivatives, and are not as likely to become habituating and are more easily administered. The sedatives are also used as a preliminary to general anesthesia and the short-acting ones are used as basal anesthetics. Because of their capacity to induce amnesia, the sedatives have been used in obstetric practice, but since the drugs enter the fetal circulation, the use of effective doses is accompanied by high fetal mortality. They are also efficient anticonvulsants and may be used to suppress convulsions due to central nervous system stimulants.

The science of pharmacology is being developed by studies which investigate drugs and their effects. Although the effectiveness and specific properties of the psychotrophic drugs can be explained with certainty only in man, a variety of psychopharmacologic tests are in use. These include the differential effects on avoidance and escape behavior and on change in group excitability. Many others have been used in screening drugs for submission to clinical trial as tranquilizers and sedative-hypnotics.

Interesting studies have been done on the taming effects of drugs on monkeys and other wild animals. The
conditioned and unconditioned responses of rats to stimuli and the inhibitory effects on self stimulation have also been investigated. Others have investigated motor function and the capacity to evoke a cataleptic state characterized by passivity and flexibility of the extremities.

Basic screening with animals is of value with any drug that is known to have interesting clinical effects on human patients and that generally seems to have similar effects on animal subjects. Because of the close association between the autonomic nervous system and the psyche, the outward signs of anxiety and emotional excitation in animals may be detected from such signs as piloerection, curving of the back, raising of the fore-paws and, in the rat, an increased rate of defecation. The inhibition or excitation of these reactions induced by conditioning the animals to some stimulus is used as a measure of the effect of the drug under testing conditions.

Other procedures utilized in the screening of drugs include their effects on electroshock, body temperature, spontaneous activity, the electroencephalogram, galvanic skin response, et cetera. Then rigorous experimental methods are used with animals to try to determine more specifically what the behavioral effects are and how they are achieved. One needs to know precisely what the behavioral effects are before trying to relate them to the results of powerful new neurophysiological and biochemical techniques.
for studying pharmacological action in the brain.

Such drug screening is predicated upon the assumption that there is a strong relationship between man and the higher animals. The differences, however, between man and the higher animals typically used in laboratory experiments are of paramount importance in determining when it is not possible to generalize with accuracy. Some studies of animal behavior suggest that the differences between the higher animals and man are more quantitative than qualitative. Such characteristics of behavior as wakefulness, locomotion, drives, discrimination, time sense, memory, mood, and the acquisition and extinction of behavior are present and available for study in both animals and man. It is not surprising, therefore, that principles of behavior derived from animal studies frequently can be applied to man, and that a good correlation often exists between the qualitative and often the quantitative responses of animals and humans to drugs influencing behavior.

Another difference between man and laboratory animals may be related to sensitivity to drugs. It has been proposed by many that man is more sensitive to drugs quantitatively than is the laboratory animal. This conception derives from the fact that most evaluative procedures used with animals measure responses that quantitatively and often qualitatively are far removed from the effects sought clinically. When more sensitive techniques are employed, which measure in
animals the same indices of change observed in the human, an
unusual degree of correspondence frequently exists, and one
can often make valid predictions for man with respect to
dosage and therapeutic ratio of drugs entirely on the basis
of animals studies. This, however, is true only when
similar procedures are employed in both animal and clinical
investigations.

Therefore, it is entirely appropriate that screening of
drugs be done with higher animals. There is the additional
incentive that clinical screening, as opposed to animal
screening, of behavioral drugs suffers from being time-con-
suming and inefficient. Clinical screening can also be
complicated by a multiplicity of extraneous variables due to
the increased complexity of the psychology of the experimen-
tal subjects. Accordingly, it is the thesis of this paper
that a specific hypnotic-sedative drug, namely Doriden, can
be evaluated better in animals than in man. Such an evalua-
tion can allow one to predict the value of the drug in the
treatment of mental disease.

The psychoactive drug Doriden is a relatively new mem-
ber of the hypnotic-sedative drug group. Investigations of
this group as a whole have produced considerable data in the
area of fetal development, the depressant effects on the
brain and their biochemical and neuro-physiological actions.
Probably the best known of the hypnotic and sedative drugs
is the teratogenic sedative thalidomide. This glutarmide
derivative has since been withdrawn from the market but was responsible for many birth defects before its tragic effects were discovered. Doriden (glutethimide) is the only other glutarimide derivative presently marketed. It has been subjected to several investigations for possible teratogenic action. However, the metabolic fates of glutethimide and thalidomide are entirely different, thalidomide being metabolized mainly by hydrolysis and glutethimide by hydroxylation. No cases of teratism involving glutethimide have been reported in humans, even though the drug has been widely used since 1955.

Related Studies

McCull, Globus and Robinson (10) investigated groups of 15 and 20 Sprague-Dawley rats placed on a diet containing the sedative-hypnotics thalidomide (1 per cent and 2 per cent), phenobarbital (0.16 per cent), methaqualone (0.8 per cent) and glutethimide (0.4 per cent). Both male and female animals received the test agent. One hundred and three pregnant animals were studied and of 233 dead offspring, 137 were examined for skeletal malformations. Offspring mortality was highest in the phenobarbital (78 per cent) and thalidomide groups (29 per cent and 42 per cent respectively) as compared to the controls (6 per cent). Mortality was less with methaqualone (23 per cent) and glutethimide (13 per cent). Litter size was decreased in the phenobarbital- and thalidomide-treated groups, suggesting uterine reabsorption.
Examinations of stained skeletons revealed abnormalities of a kind observed with other teratogens. These included multiple occurrence of double vertebral centra. This was highest with methaqualone (9/9), thalidomide 2 per cent (30/48) and phenobarbital (20/25) and lowest with glutethimide (4/17). Gross defects following glutethimide treatment were not demonstrated in this study. These results are consistent with the findings of Tuchmann-Duplessis (15) and Tuchmann-Duplessis, Mercier, and Parot (16) in investigations of fetal development in the rat, mouse and rabbit.

Electrophysiological studies (13) indicate that subtle changes occur prior to the onset of depression induced by the sedative and hypnotics. The drugs induce first a fast activity evident in the electroencephalogram with a resultant imbalance between the inhibitory and facilitatory mechanisms that normally characterize random high-voltage slow waves found in natural sleep.

Although moderate doses of the sedative-hypnotics depress the hypothalamus and prolong the recovery of the relays of the thalamic nuclei, they do not suppress the cortical response induced by stimulation of the diffuse thalamic projection system as the tranquilizing agents do. Various studies (1, 2, 7, 11) have shown that the major tranquilizers cause considerable impairment of learning, motor behavior, coordination and reaction time. It is important to note that the major tranquilizers slow the brain wave frequencies of the
electroencephalogram and do inhibit learning, while the sedative-hypnotics increase brain wave frequencies. Previous investigations indicate that at normal dosage levels the sedative-hypnotic drugs phenobarbital and secobarbital do not significantly (p = .05) inhibit learning (7, 14, 12).

A new drug of the sedative-hypnotic group has not been investigated previously in this regard. This drug is Doriden (glutethimide), a psychoactive drug which was introduced into clinical medicine as a sedative hypnotic agent in 1954 by the Ciba Pharmaceutical Company. It is a piperidinedione derivative with actions closely resembling those of the barbiturates.

The history of Doriden is similar to that of many of the newer hypnotics. On introduction, it was acclaimed as an effective "nonbarbiturate" hypnotic and sedative, free of some of the disadvantages of barbiturates and probably lacking in addiction liability. The drug gained instant and widespread acceptance, and within two years it had become one of the most popular hypnotics in the United States. A prescription survey in 1955 indicated that it was the sixth most frequently prescribed sedative, the first five being barbiturates (9). Concomitant with its rise in popularity was its rise as an agent in poisonings and fatalities. Sixty-eight cases of glutethimide poisoning, including fourteen fatalities, had been described in the medical literature by 1962 (8). The cause of these fatalities and poisonings
was misuse. Doriden, like other sedative-hypnotics, was often abused by maladjusted persons to reinforce the effects of alcohol. There is difficulty in thinking, impairment of self-control, poor judgment, emotional instability, and occasionally a toxic psychosis.

Finally, whereas the drug had been described in the literature as nonaddictive, it was later shown to be truly physiologically addictive. Withdrawal symptoms were shown to be delirium and convulsions.

The pharmacology of Doriden has been studied by Gross and associates (3, 4) and by Turrian and Gross (17). In animals the fate, metabolism and excretion of Doriden has been shown to be essentially the same as that of the other hypnotic-sedatives. Gluthethimide is a white crystalline compound with a melting point of 83-85 C and possesses a molecular weight of 217.3. It is relatively insoluble in water but easily soluble in alcohol and acetone. The drug exhibits a high lipid water partition coefficient and, therefore, penetrates diffusion barriers rapidly. When it is injected intravenously it behaves somewhat as does thipental. The concentration in the brain and other vascular tissue rises rapidly and then falls as the drug is redistributed to poorly perfused tissues. However, absorption from the gastrointestinal tract tends to be somewhat irregular, owing to the fact that the drug is so poorly soluble in water.
Glutethimide is entirely metabolized in the body. In the rat the half-life of the drug is about four hours; it is apparently much shorter in the dog, and probably also in man. A very large proportion of the metabolic products is secreted with the bile into the intestine, from which gradual reabsorption occurs. Thus, although glutethimide itself is rapidly converted in the body, its metabolites tend to be captured in the hepatic circulation. Excretion of the metabolites in the urine is therefore quite slow. In animals, glutethimide stimulates hepatic enzyme activity responsible for metabolizing barbiturates.

Koransky, Wolfgang, and Ullberg (6) investigated the distribution of glutethimide labelled with 14-C, using whole-body autoradiography. Three pregnant mice in the late gestation state (two days before expected parturition) were used as experimental animals. One of the mice was given 14C-glutethimide in water suspension by stomach tube, the second was given the preparation suspended in oil (oleum arachidis) also by stomach tube, while the third mouse was injected subcutaneously with an oil suspension.

The study showed that 14C-glutethimide given orally in water has specific uptake in liver and fat (also "brown fat"), mammary glands and Harders glands. Accumulation can also be seen probably in connection with excretion, in the nasal conchae, renal medulla, and pelvis and biliary ducts. The brain and pituitary gland of the mother show higher concentrations of 14C-glutethimide than do the skeletal muscles.
Within the brain the distribution is rather even, but slightly higher concentrations are found in grey than in white matter.

The myocardium and walls of the large arteries were shown to have higher concentrations than the skeletal muscles. The concentration in blood is lower than in the tissues, except mature bone, which shows hardly recognizable amounts of radioactivity. The level in bone marrow is similar to that of skeletal muscles.

The Korensky, Wolfgang, and Ullberg investigation further showed that the distribution of 14C-glutethimide given orally in oil is not significantly different from oral administration of glutethimide in water. The concentration of 14C-glutethimide in the liver, after subcutaneous injection, was lower than when the drug was orally administered. A relatively high amount of radioactivity was seen in the stomach and intestine after glutethimide administration. The distribution pattern is otherwise not noticeably different from that seen after oral glutethimide application.

The therapeutic applications of Doriden were found to be similar to those of the other hypnotics and sedatives. Doriden has been particularly useful as an adjunctive drug to resperine therapy. It tends to increase contact and communication, decrease attention, decrease anxiety, and decrease psychotic manifestations. Combined with interview techniques that aim at arousing emotions, strong emotional
reactions may be catalyzed for psychotherapeutic abreaction. Doriden is clearly ineffective in schizophrenia and in remedying the speech defects of true aphasics, even transiently.

Kline, Barra, and Gosline (5) have described the advantages of using Doriden as an adjunctive drug in reserpine therapy. Reserpine therapy has the disadvantage that it may be attended by states of strong and prolonged restlessness and depression. When Doriden was added to the daily medication of hospitalized patients, impressive and rapid changes in the state of health and behavior were observed in a considerable number of cases of reserpine-depression. The improvements were observed as (1) a very marked rousing effect, inasmuch as the patients had become drowsy, (2) increased drive, manifested in motility, stream of thought, and attention, (3) a less depressed mood, which could lead to a completely balanced mood or occasional euphoria, and (4) the disturbances in sleep were frequently accentuated, at least in the first days of reserpine-glutethimide medication. The change in the condition occurred within twenty-four to forty-eight hours of the introduction of Doriden and could be maintained at a constant level for days or weeks. On discontinuation of medication the depressive symptoms recurred within a few days, but the effect of the medication was reproducible by its reintroduction.
The work which has been done on Doriden, however, as summarized above, is entirely of a physiological nature concerning fate, absorption, and secretion. By contrast, the psychological effects on problem solving have not been investigated previously. An investigation into the effects of Doriden upon problem solving is appropriate, however, because it is in constant use in problem solving situations. It is, for instance, used to obtain more reliable estimates of intelligence and personality through psychological tests, particularly in emotionally upset individuals where concentration is necessary. It is also appropriate to ascertain the effects of the drug on problem solving because this facility is characteristically notable in certain neuroses and in schizophrenics.

It is pertinent to know whether an illness characterized by a decline in problem solving ability is being treated by a drug which further deteriorates problem solving ability. It is equally pertinent to know if problem solving ability is specifically improved per se. Accordingly, it is the purpose of this thesis to examine the effect of Doriden on problem solving.

Specifically, the present study was designed as an exploratory investigation of the effects of Doriden on the maze learning ability of mice. Because there is no current evidence or empirical basis for predicting change or direction of possible change, no formal hypotheses were formulated.
CHAPTER BIBLIOGRAPHY


CHAPTER II

METHOD

Subjects

The Ss were 40 experimentally naive male C57 strain, C57BL/6j descendents of mice obtained from Jackson Laboratory, Bar Harbor, Maine. They were approximately 90 to 180 days old and weighed from 17 to 35 gm. at the beginning of the experiment. They were assigned randomly to two groups and housed four to a cage with food and water available at all times. Due to the effect that environmental temperature has on the action of the tranquilizing and sedative drugs the Ss quarters were maintained at 74 degrees Fahrenheit.

Apparatus

The apparatus consisted of a galvanized metal box with outside dimensions of 12" X 24". (See Figure 1, page 17.) The interior was divided by metal partitions which created six separate compartments. The compartments were accessible by individual openings. The height of the maze was 8", and it was filled with water to a depth of 5". The maze was rinsed and the water changed daily. Water temperature was kept at a constant 80 degrees Fahrenheit by aquarium heaters. Compartment number 6 contained the escape apparatus. This was a 3" X 10" section of hardware cloth with squares measuring 5/16" X 5/16".
Fig. 1—Top View of Maze
The starting position of the Ss was in the main runway between compartments number 1 and number 2.

Drug Treatments

All Ss in the experimental group received 50mgm/kg of glutethimide thirty minutes prior to each block (four trials) of testing. The large dosage had been suggested by pilot work to be about the greatest amount that would allow for free swimming with no severe muscular incoordination. This dosage, however, produced noticeable sedation in the home cage situation.

For oral administration the tablets were ground and a suspension was heated to 100 degrees Fahrenheit for maximum distribution of the drug in the suspension. One inch of I. V. tubing was placed on the tip of a number 24 needle for oesophageal administration.

Procedure

Ss' task was to swim the water-filled maze to compartment number 6, where he climbed the escape ladder. He was then gently dried in a soft towel and placed in the home cage. Trials were given in blocks of four, with one-hour intervals between trials, for a period of four hours. The Ss received four trials a day for five successive days. Testing sessions were given at 24-hour intervals and at the same hour each day. Procedures for experimental
controls were identical except that the control received no drug prior to each block of trials.

If S responded by entering any compartment other than compartment number 6, he was credited with one error for each wrong compartment entered. In scoring maze errors the whole body (exclusive of the tail) must have entered the opening.
Presented in this chapter are the results obtained and
the statistical analyses of those results. To aid in sta-
tistical interpretation of these results, the twenty trials
of the control group and the twenty trials of the treatment
group were divided into five blocks. Each block consisted
of four trials, so that the first four trials were block one,
the second four trials, block two, et cetera. The mean
number of errors for each block is presented in Table I.
The differences between the means for controls and treatments

<table>
<thead>
<tr>
<th>Block</th>
<th>Trials</th>
<th>Mean Errors</th>
<th>Mean Difference</th>
<th>t Value</th>
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<tr>
<td>I</td>
<td>1-4</td>
<td>5.300</td>
<td>5.162</td>
<td>.137</td>
</tr>
<tr>
<td>II</td>
<td>5-8</td>
<td>5.387</td>
<td>4.225</td>
<td>1.1625</td>
</tr>
<tr>
<td>III</td>
<td>9-12</td>
<td>4.612</td>
<td>3.300</td>
<td>1.3125</td>
</tr>
<tr>
<td>IV</td>
<td>13-16</td>
<td>3.212</td>
<td>3.250</td>
<td>.0375</td>
</tr>
<tr>
<td>V</td>
<td>17-20</td>
<td>2.850</td>
<td>2.812</td>
<td>.0375</td>
</tr>
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</table>

***Significant at p < .001.
in each block were investigated for statistical significance by t test. The t values are also shown in Table I. Comparison of the t values in Table I revealed that trial blocks II and III were significant at the $p < .001$ level. Trial blocks I, IV and V were not significant at the $p < .05$ level.

To assess the effects of the drug on learning, a 2 X 2 factor analysis of variance was performed on the mean scores of the control and experimental trial blocks. Presented in Table II are the results of the analysis. The F values calculated on the mean squares in the Analysis of Variance,

**TABLE II**

**SUMMARY OF ANALYSIS OF VARIANCE OF DRUG TREATMENT AND FIVE TRIAL BLOCKS**

<table>
<thead>
<tr>
<th>Source of Variation</th>
<th>Sum of Squares</th>
<th>df</th>
<th>MS</th>
<th>F</th>
</tr>
</thead>
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<tr>
<td>Treatment with drug</td>
<td>2.1856</td>
<td>1</td>
<td>2.1856</td>
<td>4.3015*</td>
</tr>
<tr>
<td>Learning</td>
<td>32.9940</td>
<td>4</td>
<td>8.2485</td>
<td>16.2340**</td>
</tr>
<tr>
<td>Interaction</td>
<td>4.0052</td>
<td>4</td>
<td>1.0013</td>
<td>1.9706</td>
</tr>
<tr>
<td>Within</td>
<td>15.2420</td>
<td>30</td>
<td>.5081</td>
<td></td>
</tr>
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</table>

*Significant at $p < .05$.
**Significant at $p < .01$.

Table II, indicate that the main effects of the drug ($F = 4.3015$, $df = 1$, $p < .05$) and the main effect for learning ($F = 16.2340$, $df = 4$, $p < .01$) were significant, while the Drug Treatment X Learning Condition interaction was not significant at the $p < .05$ level.
In order to explore further the learning curve in the Control and Treatment groups a Student's t test was used to determine significant differences on successive trial blocks within each group. These results can be seen in Table III.

**TABLE III**

MEAN DIFFERENCES AND t VALUES FOR SUCCESSIVE TRIAL BLOCKS FOR CONTROL AND EXPERIMENTAL GROUPS

<table>
<thead>
<tr>
<th>Block</th>
<th>Mean Errors</th>
<th>Mean Difference</th>
<th>t Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>5.162</td>
<td>.937</td>
<td>7.6178 ***</td>
</tr>
<tr>
<td>II</td>
<td>4.225</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>4.225</td>
<td>.325</td>
<td>7.5203 ***</td>
</tr>
<tr>
<td>IV</td>
<td>3.300</td>
<td>.0500</td>
<td>.04065</td>
</tr>
<tr>
<td>V</td>
<td>3.250</td>
<td>.438</td>
<td>3.5609 **</td>
</tr>
</tbody>
</table>

| **Experimental Group** | | | |
| I     | 5.300       | -.913           | -7.422 |
| II    | 5.387       |                 |        |
| III   | 5.387       | .775            | 6.300 ** |
| IV    | 4.612       | 1.400           | 11.3821 *** |
| V     | 3.212       | .362            | 2.9430 ** |

**Significant at p < .05.**

**Significant at p < .001.**
The control group shows a significant ($p < .001$) reduction in the mean number of errors made on trial blocks I, II and III. The mean number of errors made on trial block IV is not significantly different from the mean number of errors made on trial block III. This leveling off is probably due to task difficulty. Trial block V shows a significant ($p < .001$) reduction in mean number of errors but here again a leveling off can be seen in Figure 2.

The experimental group does not show a reduction in the mean number of errors between blocks I and II, which would indicate that the drug has affected the learning process. Trials four through twenty (trial blocks II, III, IV and V) show a decrease in mean number of errors significant at the $p < .001$ level.
Fig. 2--Mean Number of Errors for Five Trial Blocks
CHAPTER IV

DISCUSSION

The present study suggests that Doriden administered to mice prior to a learning task will have a significant effect on learning. This effect will be a temporary impairment on problem solving ability and concentrative attention span. It is further suggested that a drug "tolerance" or drug "adaptability" level is reached after receiving the drug for several consecutive doses.

As can be seen from examining Table I, both treatment and control groups performed with about the same accuracy on trial block I, yielding no significant difference in their performance. Trial block II performance shows that the control group had a significant (p<.001) decrease in mean number of errors while the treatment group has a very slight increase in performance which is not significant at p<.05 level. Both groups show a significant (p<.001) decrease in mean number of errors on trial block III. On the fourth block of trials the treatment group showed a significant decrease in errors (p<.001) and the performance of the control group levels off. This slight decrease in mean number of errors is significant at the p<.05 level. Task difficulty should be considered here since both groups begin to show a leveling off of performance in the following trials.
Trial blocks IV and V had mean differences of .438 for the controls and .362 for the treatment group. Although this is significant at the p < .001 level, the decrease is not as significant as it was in blocks I and II of the control and II and III of the experimental.

By comparing the differences between the means in Table III it is evident that the treatment showed no decrease in mean number of errors on trial blocks I and II. The treatment group's performance began to rapidly improve on trial blocks III and IV. The treatment group's performance was not significantly different from that of the control group on trial block IV. This can be seen graphically by examining Figure 2. It is possible that the lack of error decrements on trial block II for the experimental group might be attributable to motor effects or to general sedative debilitating effects of the drug. Since it is known that the level of a subject's motivation, fear, and/or anxiety is reflected in his motor behavior, it can be shown that any alteration in his affective level will similarly produce differential motor performance. During trial blocks I and II, the drug had its maximum intoxicating effect. The animals had not acquired drug tolerance during trial blocks I and II. It is postulated that this failure to acquire tolerance was a function of a decrease in the level of motivation to find the escape solution as well as a function of an impairment of concentrative attention span and problem
solving ability. The drug, when first administered, produced a state of intoxication and as the animals built up tolerance to the drug it had more of a sedative effect and an alteration in affective level.

Kornetsky (1) investigated the effects of meprobamate, which has actions on the brain that are very similar to those of Doriden. On alternate days, eight volunteer subjects were given 300 milligrams of meprobamate and a placebo. A multiple stimulus-response apparatus was employed that allowed the measurement of a variety of types of behavior while always evoking the same motor response on the part of the subject. The apparatus consisted of a subject panel of 10 lights and 10 adjacent buttons. The apparatus was designed so that the experimenter could pair any light to any button and could program the order of stimulus lights in any sequence. The three procedures that measure three levels of behavior were studied. Procedure "A" was a simple motor response somewhat analogous to simple reaction time. Procedure "B" was a choice visual motor response analogous to choice reaction time. Procedure "C" involved simple learning in which the stimulus lights were randomly paired with the response buttons. When the comparisons were made between placebo and 300 mgm. of meprobamate trial by trial, it appeared that this dosage of the drug did impair learning. Significant differences (p .05) were found at trials 6, 7, and 8. Meprobamate caused no significant motor impairment
on procedures "A" and "B", and the initial and the final trial on learning were similar to those of the placebo, indicating that any separation of the learning curves between the placebo and this dose of meprobamate is the result of differential rate of learning.

The results of the present study are consistent with Kornetsky's (1) findings. It is now hypothesized that agents (such as Doriden, meprobamate and phenobarbital) which have a major depressant effect on the cortex as well as upon subcortical structures will significantly impair concentrative attention span, problem solving ability, and motivational level until drug "adaptability" or "tolerance" is reached. This would indicate that these agents have certain advantages over the phenothiazines, which impair concentration and attention and complicate the treatment of neuroses. This study suggests that Doriden does not impair concentration or attention once drug adaptability is obtained, and therefore aids the neurotic patient to overcome the need for repression and to promote free association.
CHAPTER V

SUMMARY

Impairment of problem solving ability and concentrative attention has been characteristically notable in certain neurotics and schizophrenics. Conversely, increased span of concentrative attention to external stimuli and increased problem solving ability are regarded as a measure of improvement. The present study was designed as an exploratory investigation of the effects of Doriden on concentrative attention span and problem solving ability in mice, as measured by a water-filled maze.

Forty experimentally naive C57BL/6J mice were used in the present study. The experimental group received 50mg/kg of Doriden thirty minutes prior to each block (four trials) of testing. The control group did not receive any drug or treatment prior to the trial blocks. S's task was to swim the water-filled maze to a compartment which had an escape ladder. Trials were given in blocks of four trials each, with one-hour intervals between trials, for a period of four hours. The Ss received four trials a day for five successive days, making a total of twenty trials for each subject. Performance was based on the number of incorrect compartments entered during the trials. The statistical analysis was done on the mean number of errors for each trial block.
The only significant differences between the control and experimental groups' performance were on trial blocks II and III. On trial blocks IV and V the experimental group's performance improved and was not significantly different from the control group's performance.

The present study suggests Doriden will not impair concentration or attention and therefore is useful in the evaluation and treatment of neuroses.
BIBLIOGRAPHY

Articles


